Published in final edited form as:

J Biomech. 2018 October 26; 80: 63–71. doi:10.1016/j.jbiomech.2018.08.030.

Harmonizing finite element modelling for non-invasive strength estimation by HR-pQCT

Danielle E. Whittier¹, Sarah L. Manske¹, Douglas P. Kiel², Mary Boussein³, and Steven K. Boyd¹

¹McCaig Institute for Bone and Joint Health and Department of Radiology, Cumming School of Medicine, University of Calgary, Calgary AB, Canada

²Institute for Aging Research, Hebrew Senior Life, Boston, MA, USA, Department of Medicine, Harvard Medical School, Boston, MA, USA, Division of Gerontology, Beth Israel Deaconess Medical Center, Boston, MA, USA

³Beth Israel Deaconess Medical Center, Center for Advanced Orthopedic Studies, Boston, MA, USA

Abstract

The finite element (FE) method based on high-resolution peripheral quantitative computed tomography (HR-pQCT) use a variety of tissue constitutive properties and boundary conditions at different laboratories making comparison of mechanical properties difficult. Furthermore, the advent of a second-generation HR-pQCT poses challenges due to improved resolution and a larger region of interest (ROI). This study addresses the need to harmonize results across FE models. The aims are to establish the relationship between FE results as a function of boundary conditions and a range of tissue properties for the first-generation HR-pQCT system, and to determine appropriate model parameters for the second-generation HR-pQCT system. We implemented common boundary conditions and tissue properties on a large cohort (N=1,371), and showed the relationships were highly linear ($R^2 > 0.99$) for yield strength and reaction force between FE models. Cadaver radii measured on both generation HR-pQCT with matched ROIs were used to back-calculate a tissue modulus that accounts for the increased resolution (61 μ m versus 82 μ m), resulting in a modulus of 8,748 MPa for second-generation HRpQCT to produce bone yield strength and reaction force equivalent to using 6,829 MPa for first-generation HR-pQCT. Finally, *in vivo* scans (N=61) conducted on both generations demonstrated that the larger ROI in the second-generation system results in stronger bone outcome measures, suggesting it is not advisable to convert FE results across HR-pQCT generations without matching ROIs. Together, these findings harmonize FE results by providing a means to compare findings with different boundary conditions and tissue properties, and across scanner generations.

Address for correspondence: Steven K. Boyd, McCaig Institute for Bone and Joint Health, University of Calgary, Room HRIC 3A16, 3280 Hospital Dr NW, Calgary, Alberta, Canada, T2N 4Z6, Phone: 403-220-3664, skboyd@ucalgary.ca.

DISCLOSURES

Steven K. Boyd PhD, is co-owner of Numerics88 Solutions Ltd. All other authors state that they have no conflicts of interest.

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Keywords

high-resolution peripheral quantitative computed tomography; bone mineral density; bone microarchitecture; bone strength; finite element analysis; micro-FE

INTRODUCTION

Finite element (FE) analysis applied to bone microarchitecture obtained using micro-computed tomography (μ CT) has become an established method to non-invasively estimate bone strength for a broad range of applications (Van Rietbergen et al., 1995). Of these, FE analysis is now commonly applied to images obtained *in vivo* from high-resolution peripheral quantitative computed tomography (HR-pQCT) to estimate mechanical properties of the distal radius and tibia (Pistoia et al., 2002, 2004). The application of linear, non-linear, and continuum-based FE models to HR-pQCT images has been explored, and is frequently referred to as micro-FE or large-scale FE. Of primary interest is linear FE models as this approach has been employed by most of the large HR-pQCT cohorts internationally, yet there has been an evolution of constitutive properties and complexities, and a range of boundary conditions applied to different study cohorts (van Rietbergen and Ito, 2015). These voxel-based methods are well suited for high-throughput analysis due to memory- and computational-efficient software, and are based on well-validated outputs (MacNeil and Boyd, 2008; Mueller et al., 2011) which typically include bone stiffness, localized tissue stresses and strains, and yield strength (Pistoia et al., 2001). However, subtle but important differences in material properties and boundary conditions make it challenging to compare results across cohort studies that are focused on understanding the relationship between bone microarchitecture and fragility fractures (Boutroy et al., 2008; Melton et al., 2007; Ohlsson et al., 2017; Sornay-Rendu et al., 2007; Stein et al., 2010; Vico et al., 2008; Vilayphiou et al., 2011). Harmonizing micro-FE results will be important so that existing cohorts can be consolidated, and conclusions can be drawn from a larger sample population.

The boundary conditions of micro-FE models are designed to apply a standardized test configuration so that intra- or inter-individual strength comparisons can be performed. Even with standardized testing, differences in selection of boundary conditions and material properties between research centers make it difficult to merge cohorts. Typical differences in boundary conditions include axial versus uniaxial constraints, where the former is constrained in the lateral directions at the contact platens (i.e. high friction) (Boutroy et al., 2008), and the latter is not constrained laterally (MacNeil and Boyd, 2008) (i.e. low friction; Figure 1). Important material properties to consider are the critical strain value (usually ranging between 3500μ and 7000μ), the tissue elastic modulus employed (ranging from 6,829 MPa to 20,000 MPa), and whether the same modulus is applied for both cortical and trabecular compartments or if mixed-compartment conditions are used for cortical bone and trabecular bone (e.g. 20,000 MPa and 17,000 MPa, respectively) (Boutroy et al., 2008). Each laboratory has specific and well-justified reasons for specifying the parameters they use in their micro-FE models, and have resulted in differences among several large cohorts including MrOs (Nilsson et al., 2017), Mayo clinic (Khosla et al., 2006), Canadian Multi-Centre Osteoporosis Study (CaMos) (Burt et al., 2016; Macdonald et al., 2011),

Framingham Osteoporosis Study (Liu et al., 2017), Os des Femmes de Lyon (OFELY) study (Sornay-Rendu et al., 2017), STRucture of the Aging Men's BOnes (STRAMBO) study (Szulc et al., 2013), and others.

Further confounding these efforts is the advent of a second-generation HR-pQCT (XCTII), which compared to first-generation HR-pQCT (XCTI), has a smaller voxel size (61 μm versus 82 μm) and larger region of interest (ROI) (10.2 mm versus 9.0 mm). Both of these factors independently affect the FE strength estimations, and must be considered when comparing study cohorts. An additional challenge is that the larger ROI of XCTII will ultimately result in different FE strength estimations because the extended ROI typically includes more bone proximally, a predominantly cortical site. The effect of the increased ROI are unclear and must be investigated if FE strength estimations are to be compared across scanner generations.

The aims of this study are to establish the relationship between different linear micro-FE models as a function of boundary conditions and tissue properties for XCTI, and to establish an appropriate tissue modulus for FE models based on XCTII. These results will provide a basis to harmonize FE results within the research field, independent of boundary conditions, selected material properties, and HR-pQCT generation.

MATERIALS AND METHODS

Boundary conditions and tissue properties for first-generation HR-pQCT

The three factors we tested that differed among a survey of major cohorts with HR-pQCT outcomes were (1) boundary conditions (uniaxial versus axial), (2) material properties (a tissue elastic modulus of 17,000 MPa and 20,000 MPa for trabecular and cortical bone, respectively, or whole bone with either 6,829 MPa or 10,000 MPa), and (3) critical strain (3500 μ to 7000 μ) for a estimating linear-based failure load (Pistoia et al., 2001).

The relationship between factors for the three conditions were determined by performing repeated analysis of linear FE models on a large cohort. Distal radius and distal tibia scans were obtained *in vivo* from 1,371 participants in the ongoing Framingham study (Samelson et al., 2018), acquired at one site using a first-generation HR-pQCT (XtremeCT, Scanco Medical, Switzerland). All image acquisition and analysis steps followed the manufacturer's standard protocols (Boutroy et al., 2005; Burghardt et al., 2010) with a fixed reference line. The scans were acquired 9.5 mm and 22.5 mm proximal from the reference line for the radius and tibia respectively. The periosteal and endosteal surfaces of the bone were found semi-automatically, and the cortical and trabecular regions were segmented. Images were then filtered with a Laplace-Hamming filter (Laplace ϵ 0.5, Hamming cut-off 0.4) and binarized using a fixed global threshold (Boutroy et al., 2005; Burghardt et al., 2010; Laib and Rueggsegger, 1999).

Three sets of FE models were analyzed to represent the factors used at different research centers. All models were defined with a 1% compressive strain applied in the axial direction (z-axis), and primary outcome measures were reaction force (N) and estimated failure load (N). The micro-FE models consist of many other outcome measures; however, these two

primary measures are linearly related to those other outcomes (e.g. von Mises stresses, principal strains, etc.). The first set of models was solved with uniaxial boundary conditions, a tissue elastic modulus of 6,289 MPa, a Poisson's ratio of 0.3, a critical strain of 7,000 μ , and critical volume of 2%. The second set of models was solved using the same tissue properties, but with axial boundary conditions. Finally, the third set of models was solved with a multi-compartment tissue modulus of 17,000 MPa for trabecular bone, and 20,000 MPa for cortical bone, axial boundary conditions, a Poisson's ratio of 0.3, and a critical strain of 7000 μ and critical volume of 2%. There was no need to solve the models with a tissue elastic modulus of 10,000 MPa because the linear conversion from models with a tissue elastic modulus of 6,289 MPa is trivial (all FE outcomes can simply be scaled by a factor of 10,000 / 6,289). Similarly, the change in strength outcomes with a critical strain of 3500 μ versus 7000 μ is linearly scalable.

The FE models were solved using a conjugate gradient approach with a convergence criteria of 1×10^{-6} (FAIM v8.0, Numerics88 Solutions Ltd, Canada) on a university computing system (Helix, dual socketed E5-2680 v3 with twelve 2.50 GHz cores, 256 GB RAM).

Linear regressions established the slope and intercept for the relationship between differing tissue moduli, boundary conditions and critical strain. The slope and intercept form the basis to estimate the conversion of models between different conditions. Bland-Altman plots were generated to determine the 95% level of agreement between differing methods used after conversions were applied.

Tissue modulus for second-generation HR-pQCT

The differences between scanner specifications for HR-pQCT generations are shown in Table 1. The difference in bone volume extracted due to these scanner specifications, and the effect of a larger ROI (10.25 mm from 168 slices versus 9.02 mm from 110 slices) independently affect the FE strength estimations. First, the effect of extracted bone volume on selection of the appropriate tissue modulus was determined. The tissue modulus for XCTI was determined by validation against cadaver mechanical testing (MacNeil and Boyd, 2008; Mueller et al., 2011), but rather than repeat the original experimental validation, we performed a direct *in silico* comparison between estimate stiffness from FE models of the same structures measured with XCTI and XCTII. We only tested radii because as per the original validation studies, it is assumed that bone tissue properties are intrinsic, and not dependent on skeletal site.

Human cadaveric radii were acquired from the University of Calgary Gross Anatomy Lab and Joint Transplant Program. Specimens were from 9 male and 11 female donors aged 49 to 95 years (mean age of 70 years). They were stored at -80°C and thawed prior to scanning. All image acquisition and analysis steps for XCTI and XCTII scans followed the standard protocol recommended by the manufacturer (Burghardt et al., 2010; Manske et al., 2015). The procedures for XCTI follow the protocol outlined in the prior section. For XCTII scans, the reference line was set at the same location as on XCTI, resulting in an extra 1 mm of bone in the proximal region of the ROI (Table 1). Similar to the XCTI protocol, the periosteal and endosteal surfaces were identified semi-automatically, and the cortical and trabecular regions segmented. In contrast to XCTI, the images were filtered using a low-pass

Gaussian filter (sigma 0.8, support 1.0) and fixed thresholds to extract trabecular and cortical bone (320 and 450 mg HA/cm³, respectively) (Manske et al., 2015).

Three-dimensional (3D) image registration (Image Processing Language, v5.42, Scanco Medical) aligned scans from XCTI and XCTII, and subsequently slices outside of the common region were removed from each pair of images to closely represent the same ROI. Using these clipped ROIs, uniaxial boundary conditions, 1% applied strain, a tissue modulus of 6,829 MPa, Poisson's ratio of 0.3, and a critical strain of 7000 μ and critical volume of 2% were applied to all models (XCTI and XCTII). A linear regression between estimated stiffness from XCTI and XCTII with an intercept passing through zero provides a best-fit scaling factor between the tissue modulus for XCTI and XCTII. BlandAltman plots were generated to determine the 95% level of agreement between the two scanner generations after the back-calculated tissue modulus for XCTII was applied. This approach to back-calculating an appropriate tissue modulus has been employed before (Boyd et al., 2002; Van Rietbergen et al., 1995), and ensures that the XCTII tissue modulus is tied to the previously completed experimental validation (MacNeil and Boyd, 2008).

Increased ROI in second-generation HR-pQCT

The effect of the larger ROI of the XCTII on estimated strength was determined using an *in vivo* dataset of 61 subjects who were scanned at the radius and tibia on both XCTI and XCTII systems on the same day. Using the tissue modulus of 6,829 MPa for the XCTI and the newly determined tissue modulus for the XCTII, we solved both models using uniaxial boundary conditions, Poisson's ratio of 0.3, and a critical strain of 7000 μ and critical volume of 2%. The linear regression and resulting slope and intercept provides a basis to estimate the difference in strength due to differences in ROI, independently from resolution effects on tissue modulus.

For all *in vivo* scanning, participants provided written informed consent prior to the involvement in the study. Approval for all procedures was obtained from the Conjoint Health Research Ethics Board at the University of Calgary for *in vitro* data and *in vivo* XCTI and XCTII data, and the Institutional Review Board for Human Research at Boston University and Hebrew SeniorLife for Framingham data.

RESULTS

The FE models varied in size depending on whether a radius or tibia was evaluated, and whether the data was obtained from XCTI or XCTII systems. A summary of the mean model sizes and solution times is provided in Table 2. The models were roughly twice as large from XCTII images and took roughly 5 times longer to solve, with an increased number of conjugate gradient iterations to solution (Jorgenson et al., 2012). A maximum of 2.5 GB and 4.0 GB RAM were used to solve the XCTI and XCTII models, respectively.

Boundary conditions and tissue properties for first-generation HR-pQCT

The relationship between FE outcomes when the two boundary conditions were used are highly linear ($r^2 > 0.99$) (Figure 2), and therefore equations that relate either mixedcompartment tissue modulus (x_{mix}) or single tissue modulus and uniaxial boundary

conditions (x_{uni}) to axial boundary conditions (y) can be determined. Axial boundary conditions are used as a reference, but any linear combination of these equations allows one to compare among outcomes. Summarized below are the relationships between axial conditions with a single modulus (6,829 MPa) with axial conditions with a mixed-compartment tissue modulus (20,000 MPa and 17,000 MPa for cortical and trabecular compartments, respectively):

$$\text{Reaction force: } y = -103 \text{ N} + 0.37x_{mix} \quad (1)$$

$$\text{Failure load: } y = -34 \text{ N} + 0.74x_{mix} \quad (2)$$

and between uniaxial boundary conditions with a single tissue modulus of 6,829 MPa and axial conditions with the same single tissue modulus:

$$\text{Reaction force: } y = 558 \text{ N} + 1.12x_{uni} \quad (3)$$

$$\text{Failure load: } y = 323 \text{ N} + 1.09x_{uni} \quad (4)$$

These relationships, which were highly linear, could be used to estimate equivalent results across boundary conditions and/or tissue moduli. Bland-Altman plots (Figure 3) indicated good agreement between axial and uniaxial boundary conditions, as well as between use of a single tissue modulus and multi-compartment tissue modulus after corrected using equations 1–4.

The conversion factor to account for a different tissue modulus when cortical and trabecular bone are treated the same is simply a linear conversion. For example, converting between a model solved with 10,000 MPa to one solved with 6,829 MPa can be done by applying a factor of 0.6829 to either failure load or reaction forces. Similarly, the effect of choosing a critical strain of 7000 μ versus 3500 μ is also a linear factor for the estimation of failure load; halving the critical strain would result in halving the failure load. Of course, the selection of a critical strain has no bearing on the reaction force or other FE outputs such as von Mises stress, etc.

All the conversions determined here are linear, and so it is possible to apply a linear combination. For example, an axial test conducted with a tissue modulus of 10,000 MPa can be converted to the equivalent outcome for a uniaxial test conducted using a tissue modulus of 6,829 MPa by combining Equations 3 and 4 with an additional factor accounting for the different tissue modulus as per above. Table 3 contains a summary of possible linear conversions.

Tissue modulus for second-generation HR-pQCT

Scans of human radii from cadavers on XCTI and XCTII were 3D registered and slice-matched to obtain similar ROIs. The matching was successful for all but two of the scans, which were discarded due to obvious poor alignment, resulting in a total of N=18 paired images. The comparison of the reaction force and failure load from XCTI and XCTII, using a tissue modulus of 6,829 MPa is shown (Figure 4). It was determined from the regression of the reaction force, which had a slope of 0.781, that the tissue modulus of 6,829 MPa used for XCTII resulted in an underestimation of the reaction force. A tissue modulus of 8,748 MPa for XCTII was established using the 6,829 MPa XCTI tissue modulus adjusted by the 0.781 factor. The reaction force is used for the modulus back-calculation because it is the primary outcome used in previous validation studies. BlandAltman plots (Figure 4) indicated reasonable agreement between XCTI and XCTII after applying the adjusted tissue modulus.

Increased ROI in second-generation HR-pQCT

Finally, we compared the reaction force and failure load using the *in vivo* scans (N=61) conducted on the XCTI and XCTII, with a tissue modulus of 6,829 MPa and 8,748 MPa, respectively. Both reaction force and failure load was greater in the XCTII scans (Figure 5) when the increased ROI and greater representation of cortical bone was included in the XCTII images. Bland-Altman plots (Figure 5) indicated bias increased with increasing failure load and reaction force.

DISCUSSION

This study established how the estimated strength characteristics from micro-FE modelling differ depending on the boundary conditions, tissue properties, and HR-pQCT generation.

Boundary conditions and tissue properties for first-generation HR-pQCT

As expected, it was found that the relationships between FE models run using different tissue properties and boundary conditions are highly linear. Bland-Altman plots (Figure 3) show a only small bias in reaction force and failure load estimates following correction, and variance in error is observed to increase with increasing failure load and reaction force, indicating a proportional difference in variability between models. Therefore it is proposed that equivalent load cases can be estimated by using the conversion equations. Together, these data provide a foundation for harmonizing microFE results across XCTI cohorts where different micro-FE models are employed to estimate bone strength. It should be noted that these relationships and conversion equations are only valid when using the manufacturer's standard protocols for XCTI scans. The equations were derived from pooled distal radius and tibia data, and the high linearity suggests that independent relationships for each skeletal site are not necessary.

There are many good rationale for choosing a tissue modulus or boundary condition utilized in the FE models, and the range of choices across research labs varies significantly. Applying a tissue modulus of 17,000 MPa for trabecular bone and 20,000 MPa for cortical bone clearly results in higher strength outcomes than models that use lower tissue modulus, as confirmed by the slopes determined in Figure 2. The choice of axial versus uniaxial

boundary conditions also has an impact on primary outcomes. When evaluated independently, the ability to draw conclusions about the estimated strength measures on a particular study question is not affected, as long as a particular cohort is consistent in the application of the FE method. However, when merging cohorts, it is important to generate consistent results, and because the correlations are highly linear and well correlated ($r^2 > 0.99$), it would appear that conversions based on the methods proposed are reasonable.

Tissue modulus & increased ROI for second-generation HR-pQCT

We back-calculated an appropriate tissue modulus for XCTII by scaling the tissue modulus for XCTI, which is tied to the validated cadaver testing that was previously performed on XCTI. Even with the adjusted tissue modulus, it was shown that the larger ROI of XCTII scans results in a greater failure load and reaction force compared to XCTI (Figure 5). These results indicate it is likely not possible to convert XCTI strength estimations to XCTII results when the larger ROI is taken into consideration.

Comparison of FE estimated strength measures between generations of HR-pQCT are confounded by both the bone volume extracted and ROI size, and this results in a complex situation for harmonizing results. The increased resolution of XCTII affects the extracted bone volume for a given region because the resolution difference allows for direct extraction of trabecular structure, instead of derived measures. The proximity of the XCTI and XCTII resolution to trabeculae structure, impacts extracted bone volume, and necessitates the use of a higher tissue modulus for XCTII scans to obtain the same estimate bone strength as found using the XCTI system, when a matched ROI is used. **In addition to differences in bone volume fraction, FE results are sensitive to element size relative to the structure being modelled. As demonstrated by Niebur (1999), a ratio of mean trabecular thickness to element size of four is required to obtain convergence behaviour in micro-FE models (Niebur et al., 1999). Resolution of XCTII and XCTI are at the cusp of meeting this criterion, but trabecular thickness at a given skeletal site, or for a given individual is variable. These differences impact FE results, and contribute to some of the variance observed when converting between XCTI and XCTII, as seen in Figure 4. Although estimation of different tissue modulus based on site, sex, or other factors correlated with trabecular thickness could be explored, here we assume the effect of these differences on FE results are relatively small, thus proposing a single tissue modulus of 8,748 MPa for use in all individuals. Estimation of this modulus carries over assumptions from our original cadaveric validation (MacNeil and Boyd, 2008), while accounting for the different scanner specifications and resultant difference in bone volume of the XCTII system. Following the same logic, the conversion of the 10,000 MPa tissue modulus often used for XCTI could also be performed by the same approach, and would result in a modulus of 12,811 MPa for XCTII. The use of the adapted tissue modulus maximizes the ability to carry forward what has been well established for first-generation HR-pQCT.**

The challenge remains for XCTII that even with an adapted tissue modulus, the larger ROI poses a problem in comparing strength estimations across scanners. It may never be possible to generate an acceptable approach to accommodate for this difference because new bone is assessed that had not previously been included on XCTI systems. We roughly estimated

from our *in vivo* data acquired on the same people on both systems that the failure load is increased by 16.3% and the reaction force is increased by 19.2%. However, as opposed to the other differences in micro-FE models addressed, the increased ROI is not a numerical problem founded in boundary conditions or model parameters, but rather a biological problem founded in the inclusion of a different ROI. Based on this information, it is likely not possible to compare strength estimations across HR-pQCT generations, despite use of the back-calculated tissue modulus to account for the improved resolution. If comparisons between XCTI and XCTII are imperative, then the ROI used in the FE model from the XCTII data should be reduced to match the XCTI ROI, and the back-calculated tissue modulus used.

Limitations of this study include the relatively small number of cadaveric scans used to back-calculate the tissue modulus used for XCTI and XCTII; however, it is prohibitively time consuming and costly to prepare additional tissues. Another challenge was defining identical ROIs on the cadaver scans. Although the alignment was high between systems, any oblique angular differences had to be ignored so that parallel surfaces were maintained for FE modelling. The higher scatter of FE outcomes in the cadaver specimens compared to the *in vivo* measures (Figure 2) is likely a result of slight differences in ROI, but also due to the relatively smaller range of bone strengths represented, thus magnifying the effect. Another factor, for *in vivo* dataset used to compare XCTI and XCTII, are the motion artifacts that can reduce the ability to compare across conditions.

In conclusion, micro-FE model results from XCTI can be adjusted post-analysis to account for differences in tissue modulus, boundary conditions, and failure criteria; however, the increased ROI of XCTII does not make it advisable to convert across generations of systems. Nevertheless, a tissue modulus that accounts for the scanner specification differences and resultant differences in bone volume of the XCTII has been established. Together these findings will help harmonize micro-FE results across XCTI cohorts and across generations of HR-pQCT.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the input and continuing collaboration with our international colleagues leading studies including CaMos, Framingham Osteoporosis Study, Gerico, Mayo Clinic, OFELY, QUALYOR, STRAMBO, and MrOS Sweden. Thank you to the Research Computing Services at the University of Calgary for providing access to the Helix computational cluster. Thanks to the team conducting our Calgary Vitamin D trial, which provided the *in vivo* dataset measured on both systems, and to Mark Frayne for the assistance in the image registration. Research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R01 AR061445. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Figure 1.

Uniaxial versus axial boundary conditions. While both methods include application of a fixed displacement to the top surface (usually 1% strain), the bottom surface is constrained in only the z direction (uniaxial) or fully constrained in x, y and z (axial). With permission, from Numerics88 Solutions Inc: <http://www.numerics88.com/documentation/faim/8.0/manual/>.

Figure 2.

In vivo scans (N=1,371) were solved to determine regressions of the failure load (left) and reaction force (right) by FE analysis between differing model conditions. Models with uniaxial boundary conditions and single tissue modulus ($E = 6,829$ MPa) or multi-compartment ($E_{\text{cort}} = 20,000$ MPa, $E_{\text{trab}} = 17,000$ MPa) are compared to models with axial boundary conditions and single tissue modulus ($E = 6,829$ MPa). The slope and intercept, as well as the r^2 for the regression is shown for each condition. The dotted line represents a slope of 1.0.

Figure 3. Bland-Altman plots of the failure load (left) and reaction force (right) assessed using the models described in Figure 2 after applying the conversions in equations 1–4. The solid black line represents the mean difference and the black dotted lines indicate the 95% confidence intervals.

Figure 4.

Using cadaveric scans (N=18), a regression and Bland-Altman plots of the failure load (top) and reaction force (bottom) by finite element analysis under conditions of uniaxial loading for matching ROIs from first generation (XCTI) and second generation (XCTII) scans. Both XCTI and XCTII models used a tissue modulus of 6,829 MPa. On regression plots, the r^2 and slope of the regressions are shown, where the slope represents the linear scaling factor between the tissue modulus for XCTI and the appropriate tissue modulus for XCTII. The blue dotted line represents a slope of 1.0. On Bland-Altman plots, the black dotted line represents the mean difference and the black dotted lines indicate the 95% confidence intervals.

Figure 5.

Using *in vivo* scans, a regression and Bland-Altman plots of the radius failure load (top) and reaction force (bottom) by FE analysis under conditions of uniaxial loading for first generation (XCTI) and second generation (XCTII) scans. XCTI models use a tissue modulus of 6,829 MPa on a scan length of 9.02 mm, and XCTII models use a modulus of 8,748 MPa on a scan length of 10.25 mm. On regression plots, the r^2 and slope of the regressions are shown. The blue dotted line represents a slope of 1.0. On Bland-Altman plots, the black dotted line represents the mean difference and the black dotted lines indicate the 95% confidence intervals.

Table 1.

HR-pQCT scanner specifications for first generation (XCTI), and second generation (XCTII) standard *in vivo* protocol.

Scanner	Energy (kVp)	Current (μA)	FOV (cm)	Samples	Projections/ 180°	Integration time (ms)	Isotropic voxel size (μm)	Scan time (min)	Stack length (mm)
XCTI	59.4	900	12.6	1536	750	100	82.0	2.8	9.020
XCTII	68.0	1470	14.0	2304	900	43	60.7	2.0	10.197

Table 2.

Finite element model solution parameters indicating average model size and range (min, max) in elements and nodes (millions), number of iterations to convergence (1e-6), and average solution time and range.

	Elements [M#]	Nodes [M#]	Iterations [#]	Solution time [hr:min:ss]
82 μ m models				
Radius	1.99 (1.33, 3.67)	2.95 (1.89, 5.43)	3028 (1876, 6565)	0:06:35 (0:03:16, 0:14:05)
Tibia	4.68 (3.37, 8.64)	6.97 (4.78, 13.39)	4009 (2736, 6653)	0:19:17 (0:10:35, 0:36:29)
61 μ m models				
Radius	4.58 (2.75, 9.21)	5.88 (3.49, 12.02)	7501 (2644, 15769)	0:28:50 (0:11:39, 0:56:43)
Tibia	11.50 (7.77, 21.81)	14.96 (10.22, 28.96)	7547 (3756, 16178)	1:14:13 (0:39:48, 2:29:23)

Table 3.

Constants for linear equations are provided to convert FE results for a selection of cohorts of first generation (XCTI) scans into an equivalent FE test with axial boundary conditions, an elastic modulus of 6,829 MPa, a Poisson's ratio of 0.3, and a critical strain of 7,000 μ . A summary of the FE parameters used by each cohort is provided, including boundary condition (BC), elastic modulus (E), and linear failure parameters (Pistoia). By simulating these conditions on the 1,371 datasets, the slope (m) and intercept (b) for converting reaction force and failure load results for radius and tibia scans from each XCTI cohort is listed.

				Reaction force		Failure load	
Cohort	BC	E [MPa]	Pistoia	Slope, m	Intercept, b	Slope, m	Intercept, b
CaMos	Uniaxial	6829	2%, 7000 μ	1.12	558	1.09	323
GERECO	Axial	10000	2%, 7000 μ	0.6829	0.0	0.6829	0.0
OFELY	Axial	20000, 17000	2%, 3500 μ	0.3700	-103	0.7400	-34
STRAMBO	Axial	20000, 17000	2%, 3500 μ	0.3700	-103	0.7400	-34
GOOD (Sweden)	Uniaxial	10000	2%, 7000 μ	0.7512	558	0.7512	323
MrOs (Sweden)	Uniaxial	10000	2%, 7000 μ	0.7512	558	0.7512	323
Framingham Osteopor Study	Axial	6829	2%, 7000 μ	1.000	0.0	1.000	0.0